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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/770,885

02/02/2004

Karl Y. Hostetler

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DLA PIPER US LLP

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EXAMINER

MAEWALL, SNIGDHA

ART UNIT

PAPER NUMBER

1615

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10/18/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

Application No.

10/770,885

Applicant(s)

HOSTETLER ET AL.

Examiner

Snigdha Maewall

Art Unit

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1,5-12 and 14-41 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,5-12 and 14-41 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 08/01/2007.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_.

## DETAILED ACTION

### *Summary*

1. Receipt of IDS, applicant's Arguments/Remarks and amended claims filed on 08/01/2007 is acknowledged.

Claims 1, 5, 6, 16 and 22-24 have been amended. Claims 2-4 and 13 have been cancelled. New claims 25-41 have been added. Accordingly, claims pending in this application are 1, 5-12 and 14-41.

Claim rejections under 35 USC 112.2 have been withdrawn in view of Applicant's amendment to the claims.

### *Claim Objections*

2. The amended claims 1 and 27 have been written in an incorrect Markush language. The phrase "wherein the pathological condition is selected from **a**" shall be written as "wherein the pathological condition is selected from **the**". Examiner points to the following cited in MPEP.

A Markush-type claim recites alternatives in a format such as "selected from the group consisting of A, B and C." See *Ex parte Markush*, 1925 C.D. 126 (Comm'r Pat. 1925). The members of the Markush group (A, B, and C in the example above)

***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 5-12 and 14-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amended claims 1, 22, 23, 25, 26 and 27 recite the limitations "eye trauma" and "scratching". Recourse to the specification does not reveal the presence of such recitation. This is a new matter rejection.

***Claim Rejections - 35 USC § 102***

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 5-12, 14-15 and 22-26 are rejected under 35 U.S.C. 102(a) as being

anticipated by Cheng et al. (Feb. 2002) (herein onwards Cheng et al. I).

(Investigative Ophthalmology & Visual Science, Feb. 2002, Vol. 43).

Cheng et al. disclose the intraocular drug delivery system using the free crystalline lipid prodrug of ganciclovir, HDP-P-GCV, as a prototype. Cheng et al. discloses a local intravitreal drug administration for vitreoretinal diseases, which bypasses the blood-ocular barriers and allows higher intraocular drug levels and avoids many side effects associated with systemic therapy. The intraocular drug delivery may also provide constant and slow release drug. Cheng et al. further disclose that surgical placement and replacement of intravitreal implants can cause significant adverse effects, including vitreous hemorrhage, retinal detachment, and endophthalmitis. Cheng et al. disclose that the intravitreal injection of a long-acting drug preparation would be less invasive than surgery and thus in order to prove such, Cheng et al. have demonstrated in the article that crystalline HDP-P-GCV in the form of 8- to 43-micrometer particles may have utility in treating or preventing HSV retinitis when injected intravitreally as Infrequently as once a month or less frequently (see page 515, paragraph, 5 and column 2, first paragraph). The local retinal or lens toxicity observed with high doses may be eliminated, and antiviral duration could even be prolonged by using smaller drug particles, which may provide a better release rate and require less drug to maintain a therapeutic vitreous level with the advantage of a smaller drug depot (see page 521, 4<sup>th</sup> paragraph and column 2, first paragraph).

**Response to Arguments**

7. Applicant's arguments filed 08/01/2007 have been fully considered but they are not persuasive. "Applicants argue that the references do not anticipate the claims, claim 1 as amended, now include limitations requiring that the method be used for the treatment of "macular degeneration, eye trauma, or retinal detachment." Neither Cheng I nor Cheng II explicitly teaches or inherently describes such treatments. All that is taught in both Cheng references is using the compounds, such as HDP-P-GCV (1-O-hexadecylpropanediol-3-phospho-ganciclovir) for the treatment and/or prevention of the viral retinitis, i.e., cytomegalovirus (CMV) infection of the retina.....combining references".

These arguments are not persuasive because cheng's references teach that surgical placement and replacement of intravitreal implants can cause significant adverse effects, including vitreous hemorrhage, retinal detachment, and endophthalmitis. Cheng et al. disclose that the intravitreal injection of a long-acting drug preparation would be less invasive than surgery and thus in order to prove such, Cheng et al. have demonstrated in the article that crystalline HDP-P-GCV in the form of 8- to 43-micrometer particles have utility in treating or preventing HSV retinitis when injected intravitreally as infrequently as once a month or less frequently (see page 515, paragraph, 5 and column 2, first paragraph). Further, Applicants have amended the claims to include the limitation "eye trauma". Retinitis can be characterized as one of the conditions of eye trauma, therefore, Chengs references anticipate the claimed limitations.

8. Claims 1, 5-12, 14-15 and 22-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Cheng et al. (May 2000). (Investigative Ophthalmology & Visual Science, May 2000, Vol. 41, No. 6).

Cheng et al. disclose that Cytomegalovirus (CMV) infection of the retina is the most common infection in acquired immune deficiency syndrome (AIDS) patients. (See page 1523, first paragraph).

Ganciclovir (GCV) was the first drug to be approved for CMV infection in AIDS patients. Ganciclovir is effective in treating CMV retinitis by intravenous administration, but the drug does not eliminate the virus from the retina, requiring long-term suppressive maintenance therapy. Systemic toxicity such as bone marrow suppression was also a problem. The sustained-release GCV implant is effective treatment for CMV retinitis and recurrent CMV retinitis, but complications from surgery such as endophthalmitis and retina detachment are sight threatening. Therefore, in an effort to overcome the disclosed threat, Cheng et al. developed a simple, in-office injectable local therapy that would be effective, minimally toxic, and long-lasting for treatment of CMV retinitis (page 1523, column 2, paragraph 2 and 3).

Cheng et al. further disclose the experimental treatment efficacy of 1-O-hexadecylpropanediol-3-phospho-ganciclovir (HDP-P-GCV (see figure 1 and section under pathologic evaluation of the retinitis, page 1524) and disclose that the antiviral agent, HDP-P-GCV, may be very useful as a local therapy for treating CMV retinitis, HSV retinitis, and other intraocular viral infections in both immunocompromised and

immunocompetent individuals. This type of self-assembling liposomal prodrug provides a prototype for intraocular drug delivery and may be applied to the delivery of many currently available drugs for chorioretinal or vitreoretinal diseases (page, 1531, last paragraph).

### **Response to Arguments**

9. Applicant's arguments filed 08/01/2007 have been fully considered but they are not persuasive. Applicant argues ""Applicants argue that the references do not anticipate the claims, claim 1 as amended, now include limitations requiring that the method be used for the treatment of "macular degeneration, eye trauma, or retinal detachment." Neither Cheng I nor Cheng II explicitly teaches or inherently describes such treatments. All that is taught in both Cheng references is using the compounds, such as HDP-P-GCV (1-O-hexadecylpropanediol-3-phospho-ganciclovir) for the treatment and/or prevention of the viral retinitis, i.e., cytomegalovirus (CMV) infection of the retina.....combining references".

These arguments are not persuasive because Cheng's references discloses the experimental treatment efficacy of 1-O-hexadecylpropanediol-3-phospho-ganciclovir (HDP-P-GCV) (see figure 1 and section under pathologic evaluation of the retinitis, page 1524) and disclose that the antiviral agent, HDP-P-GCV, may be very useful as a local therapy for treating CMV retinitis, HSV retinitis, and other intraocular viral infections in both immunocompromised and immunocompetent individuals. Further, Applicants have amended the claims to include the limitation "eye trauma". Retinitis can be

characterized as one of the conditions of eye trauma, therefore, Chengs references anticipate the claimed limitations.

***Claim Rejections - 35 USC § 103***

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. Claims 16-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over (Cheng et al.) or (Cheng et al. I); (Investigative Ophthalmology & Visual Science, May 2000, Vol. 41, No. 6 and Feb. 2002, Vol. 43) as cited above in view of Unger (US Patent No. 6,120,751).

The teachings of Cheng et al. have been discussed above. Cheng et al. do not exclusively teach various nucleosides, antibody or AZT.

Unger discloses compositions comprising charged lipids, targeting ligands and the use of such compositions in drug delivery, targeted drug delivery, therapeutic imaging and diagnostic imaging as well as their use as contrast agents (abstract). The composition comprises various nucleosides, antibody, polyclonal antibody, fab fragments and AZT (column 45 and 46, lines 67 and 1 and column 48, lines 18-25).

It would have been obvious to the one of ordinary skilled in the art at the time the invention was made to incorporate various therapeutic agents such as various nucleosides as cited above in the formulation of Cheng et al. since Cheng et al. suggest

that assembling liposomal prodrug provides a prototype for intraocular drug delivery and may be applied to the delivery of many currently available drugs for chorioretinal or vitreoretinal diseases and Unger teaches that such a composition comprising nucleosides help in targeted delivery. A skilled artisan would have had a reasonable expectation of success in treating pathological condition of ocular tissue with a composition comprising therapeutic agents such as nucleosides.

### **Response to Arguments**

12. Applicant's arguments filed 08/01/2007 have been fully considered but they are not persuasive. Applicant argues that there is no motivation to combine the references. Examiner points that In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, In the instant case, Unger's reference has been combined with Cheng's reference. Cheng's reference teaches treatment of retinitis with the claimed therapeutic agent and the moiety. Unger's reference teaches various drugs as claimed in the instant application. Since the therapeutic drugs claimed are nucleoside derivatives, it would

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have been obvious to the one of ordinary skilled in the art to substitute various drugs from Unger's reference as claimed in the instant application in Cheng's reference with an expectation of the nucleoside forming a complex with the claimed moiety and behaving in the similar way as taught by Cheng et al. in treating retinitis or eye trauma with a reasonable expectation of success based on the guidance provided by Cheng et al.

13. Claims 27-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over (Cheng et al.) or (Cheng et al. I); (Investigative Ophthalmology & Visual Science, May 2000, Vol. 41, No. 6 and Feb. 2002, Vol. 43) as cited above in view of Unger (US Patent No. 6,120,751) and further in view of Cundy et al.(Gilead sciences) and Hostetler et al. (antimicrobial agents and chemotherapy).

The teachings of Cheng et al. have been listed above. Cheng et al. do not teach the specific drug cidofovir and acyclovir however, Cundy et al. discloses a study that was designed to evaluate the intraocular distribution and metabolism of the antiviral nucleotide analogs cidofovir followinh intravitreal administration (abstract). Cundy et al. discloses that CMV retinitis is a viral infection which is found in patients having AIDS. The untreated disease can lead to loss of vision. The article discloses that clinical efficacy of intravitreal cidofovir (see page 570, 3<sup>rd</sup> paragraph).

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Hostetler discloses alkoxyalkyl esters of cidofovir and cyclic cidofovir, which play an important role in showing antiviral activity against cytomegalovirus in in-vitro studies (title and full article).

It would have been obvious to the one of ordinary skill in the art to substitute cidofovir or acyclovir (nucleotide or nucleoside analog/drugs as taught by Cundy et al. and Hostetler et al. in Cheng's reference with an expectation of the nucleoside forming a complex with the claimed moiety and behaving in the similar way as taught by Cheng et al. in treating retinitis or eye trauma. Based on the teachings of Cundy et al. and Hostetler et al. and the guidance provided by Cheng et al., one skilled in the art would have had a reasonable expectation of success in treating retinitis/ eye trauma with cidofovir or acyclovir or any other nucleoside complexed with the claimed moiety.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Snigdha Maewall whose telephone number is (571)-272-6197. The examiner can normally be reached on Monday to Friday; 8:30 a.m. to 5:00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Snigdha Maewall

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Gollamudi S. Kishore, PhD  
Primary Examiner  
Group 1600